Update of FDA Regulation of TDM and PGx Diagnostics -- old programs; new perspectives

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MEDICAL DEVICE AMENDMENTS OF 1976

General Controls

- Register and List
- Follow good manufacturing practices
- Report device failures

General Controls

- Inventory of tests on the market
- Tools to require good manufacturing practices
- System for remedying device failures

Premarket Review

- Division of Clinical Laboratory Devices (DCLD)
- 60 scientists

Submissions Reviewed

- Premarket Notification 510(k)s
- Premarket Approvals (PMAs)

Semantic Framework

- Old vs. New
- In vitro diagnostic devices

510(k)s

- ~ 600 submissions/year
- Substantially equivalent
- Comparisons to predicate device

510(k) Reviews

- Accuracy
- Precision
- Analytical sensitivity
- Analytical specificity

Limitations in Review

- Paper review
- Lack of performance standards

PMA Review

- ~ 6 - 12 applications/year
- Safety and Effectiveness

Clinical Performance Characteristics

- Clinical sensitivity
- Clinical specificity
- Predictive values

Limitations of Review

- Lack of “gold standards”
- Overt and latent bias
- Lack of performance standards

Scientific Model

- Literature
- Voluntary Standards
- FDA guidances

Development of a Scientific Model

- Upfront design of the study
- Careful and meticulous collection of data
- Sound interpretation of results

Quantitative Tests

- Bias or inaccuracy
- Precision
- Experiments for sensitivity and specificity

Qualitative Tests

- Cut-off points
- Equivocal zones

FDA Review

- Not outcome oriented
- Usually concurrent not prospective
- Good science/ good labeling

New Initiatives

- Least Burdensome Review Process
- Strategic Plan
- Pharmacogenomics Outreach

FDAMA

- Improved market access
- Least burdensome pathways
- Premarket to postmarket balance
- Increased interaction with industry

Least Burdensome

- Appropriate questions
- Appropriate thresholds
- Non-academic pursuits

Least Burdensome

- Matter of law
- Matter of policy
- Matter of spirit

Least Burdensome

- Two Guidance Documents
- Systems Approach
- Review Guidance

Least Burdensome

- Review changes are profound
- Parallel genetics initiatives

Least Burdensome

- Shift to data summaries
- Shift to more focused labeling review
- Shift to use of clinical literature
- Shift to postmarket analysis

Strategic Plan -- Goals

- Mission related
- Total Product Life Cycle
- Knowledge Management

Intellectual Appeal

- Premarket review limitation
- Outdated law
- Snapshot approach
- Impact of scale-up
- Impact of widespread-use

Intellectual Appeal

- Postmarket review strengths
- Quality system regulations
- Product only as good as up-front design

Quality System Regulations

- Good science
- Quality systems
- Process controls
- Verification and validation

Intellectual Appeal

- Need for harmonization
- IVD directive
- JCTLM
- NIST/NCI/CAP iniatives

TPLC IVD Pilot

- Ideal target
- Stereotyped review issues
- Cadre of like-minded scientists
- Rapidly emerging technologies
- Already multi-tasking

Office of IVDs

- Single organizational unit
- Premarket
- Compliance
- Postmarket
- One stop shopping

Office of IVDs

- Objective – TPLC
- Common technical base
- Faster response times
- Flatter more dynamic organization

Goals

- Increased transparency
- Uniform least burdensome approach
- Expedited technology transfer
- Improved connectivity and quality of work

Knowledge Based Initiative

- Internal sharing
- External sharing
- IVD web page

TDM/Pharmacogenomics

- Unusual regulatory challenges
- Analytical production of system
- Interpretation of complex data
- Risk of clinical studies

Hackett Initiative

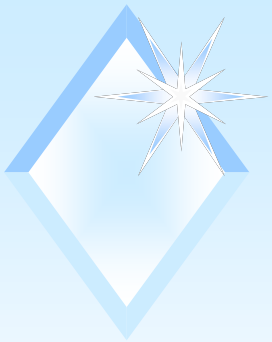
- Comprehensive outreach program
- Development of guidance
- Pharmacogenomics Round Table
- TDM Round Table
- Hunt is on!

Ongoing Issues

- Use of clinical literature
- Appropriate statistical models
- Driving submissions in

FDA Dual Mission

- Allow rapid access to good new technology
- Prevent bad products from being marketed
- Obvious inherent tension
- Strategic plan one solution
- TDM/Pharmacogenomics testing obvious model



GOOD SCIENCE